REMARKS

With entry of this amendment, claims 45-67, 69-76 and 81-87 are under consideration. Applicants have canceled claims 68 and 88 without disclaimer of or prejudice to the subject matter recited therein. Applicants have amended claims 45, 46, 50, 51, 54-56, 60, 61, 64, 81, 82-84, and 87 solely to facilitate prosecution. Support for these amendments may be found in the specification, for example, at page 22, first full paragraph. These amendments do not introduce new matter.

The Examiner has withdrawn all of the previous rejections and asserted new rejections under 35 U.S.C. §§102 and 112, which the Examiner believes were necessitated by Applicants' prior claim amendments. Applicants respond to each current rejection according to its statutory origin.

Rejection Under 35 U.S.C. § 112

The Examiner rejects claims 45-54, 65-69, 81, 82, and 85-88 under 35 U.S.C. § 112, first paragraph. According to the Examiner, the "at a differing rate in the presence or absence of said activity, wherein said activity is not part of the product" in independent claims 45, 46, and 50 lacks support in the specification. Applicants address this rejection in the context of independent claims 45, 46, and 50 as currently amended.

"At a differing rate in the presence or absence of said enzyme or factor"

Applicants respectfully remind Examiner that a claimed concept need not find verbatim support in the specification, as long as the skilled artisan would conclude that the inventors invented the claimed concept at the time of filing based on the specification's disclosure. The specification does support this concept at several locations. For example, at page 22, first full paragraph, the specification teaches that

the invention can measure factors that influence enzyme activity such as inhibitors, activators, and deactivators. Moreover, at page 16, third line from the bottom, the specification teaches that enzyme cofactors can be measured by the invention. The skilled artisan would know that these factors and cofactors can and do affect the rate of an enzyme's activity. Thus the rate of joining would be different in the presence or absence of the factor or cofactor. Indeed, at page 18, top paragraph, the specification provides an example of measuring the activity of a substance that affects the rate of activity of another. Specifically, Factor Xa can be measured in a sample by its ability to convert prothrombin into the active enzyme thrombin. Thus, Factor Xa presence is measured by cleavage of thrombin substrate. See also Example III.

Also, an enzyme may affect the rate of joining just by its presence in the sample. For example, two substrates may have the ability to join, but do so very inefficiently on their own. An introduced enzyme could quicken the joining rate of the two substrates by, for example, lowering the activation energy threshold needed to allow joining.

In sum, the specification clearly contemplates using the invention to detect an enzyme or a factor that modifies the rate of joining a first substrate to a second substrate.

"Wherein said enzyme or factor is not part of the product"

In the prior response, Applicants cited the specification at page 5, lines 1-2 and 13-14 that teaches methods for measuring the amount of an enzyme's activity that catalyzes the cleavage of a molecule or that catalyzes the joining of two or more molecules. In both methods, the activity is not bound to the product. Indeed, enzymes, as catalysts, do not remain attached to their substrates after completion of the reaction,

else they would not be able to move on to the next reaction and would be good for a single use. See, e.g., Molecular Biology of the Cell (Bruce Alberts et al., eds., 2nd edition, Garland Publishing, 1989) at page 62. Factors that effect enzyme activity act on the enzyme, not the product.

Because the rejected claims are supported by the specification, Applicants respectfully request withdrawal of the rejection of claims 45-54, 65-69, 81, 82, and 85-88 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 102

The Examiner rejects claims 45-47, 50-69, and 81-88 under 35 U.S.C. § 102(b) in light of Leland et al. (EP 570518). The Examiner alleges that the method disclosed on page 6, lines 10-26 of Leland anticipates independent claims 45 and 46. The Examiner also believes that Leland teaches that the first substrate is linked to a luminescent label and the second substrate is linked to an electrode; that the second substrate is linked to the electrode via avidin; that the first substrate comprises peptides and nucleic acids; that the electrode is linked to one or more additional substrates forming a patterned array on the electrode; and that the activity results in covalent bond cleavage and the activity is selected from the group consisting of proteases. Applicants traverse this rejection.

Regarding independent claims 45, 46, and 50, the assay quoted by the Examiner at page 6 is a binding assay, to detect the presence of an analyte by binding to assay performance substances. In contrast, claims 45, 46, and 50 recite assaying a sample for "an enzyme that modifies the rate of joining a first substrate with a second substrate to form a product or for a factor that affects the activity of said enzyme." In the case of

an enzyme, the end readout in the claimed methods is the catalytic activity of joining two substrates, an enzymatic activity. In the case of a factor, the end readout is still an enzymatic activity, the activity of the enzyme affected by the factor. Leland's assay simply measures binding, not enzymatic activity. Applicants believe that the Examiner incorrectly equates binding with enzymatic activity. See Office Action at p. 4, line 6. An analyte can bind and have no enzymatic activity. Thus, the methods of Leland and the methods of the rejected claims detect different things.

Regarding independent claims 55, 56, and 60, the Examiner's citations to Leland in support of a cleaving step do not apply. See Office Action at page 5. The Examiner's cite to page 32, line 17 recites "incubating said composition to form a complex which includes a particle and said label compound." This cite has nothing to do with a cleaving reaction. The Examiners also cite to page 11, lines 36-52, believing that it implies a cleavage reaction because the specification allegedly teaches that an amine can act as a reducing agent. This part of the specification actually describes how a co-reactant works to excite an ECL label into emitting light. Via an electron transfer, the amine group in the co-reactant interacts with an oxidized ECL label and causes the ECL label to enter an excited state from which a detectable signal comes. As describe in Leland, the reduced amine has nothing to do with facilitating a cleavage reaction as the Examiner suggests.

In sum, the Examiner has not pointed to a teaching in Leland that describes a method of assaying a sample for an enzyme that cleaves a substrate or a factor that affects the activity of the enzyme. As with claims 45, 46, and 50, Leland's binding assay is not detecting an enzymatic activity, it merely detects binding. Applicants

respectfully request the reconsideration and withdrawal of the rejection of claims 45-47, 50-69, and 81-88 as anticipated by Leland.

The Examiner rejects claims 45-54, 65-69, 81, 82, 85, 87, and 88 under 35 U.S.C. § 102(e) in light of Massey et al. (U.S. Patent 5,866,434). With respect to independent claims 45-46 and 50, the Examiner alleges that the methods disclosed in col. 13, lines 9-54, anticipate independent claims 45-46 and 50. The Examiner believes Massey teaches that the first substrate is linked to a luminescent label and the second substrate is linked to an electrode; that the second substrate is linked to the electrode via avidin; that the electrode is linked to one or more additional substrates forming a patterned array on the electrode; that the first substrate comprises peptides and nucleic acids; that the electrode comprises conductive particles in or on a polymeric material; that the activity is an enzymatic activity such as glucosidase or dehydrogenase; that the electrode comprises elemental carbon in the form of graphite; the formation of a covalent bond; and a method comprising an inhibitor.

Massey describes a binding assay where the analyte of interest remains bound to the assay-performance-substance. *See* Massey, col. 13, lines 9-57. In contrast, claims 45, 46, and 50 recite assaying a sample for "an enzyme that modifies the rate of joining a first substrate with a second substrate to form a product or for a factor that affects the activity of said enzyme." The end readout in the claimed methods is the catalytic activity of joining two substrates, an enzymatic activity. Massey's assay simply measures binding, not enzymatic activity. The Examiner has again inappropriately equated binding with enzymatic activity (Office Action at page 6, line 2). An analyte can

bind and have no enzymatic activity. Thus, the methods of Massey and the methods of the rejected claims measure different activities.

Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 45-54, 65-69, 81, 82, 85, 87, and 88 as anticipated by Massey.

Conclusions

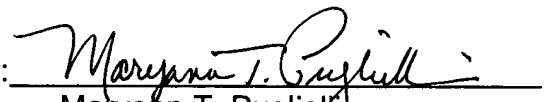
In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of claims 45-67, 69-76 and 81-87.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: December 7, 2005

By: 
Maryann T. Pugliell
Reg. No. 52,138